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[Title of Invention]

An apparatus to separate components of liquid samples.

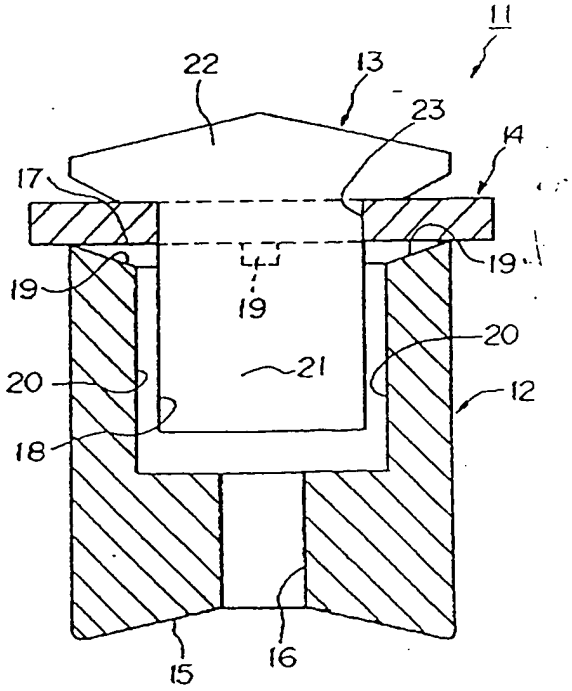
[Summary]

[Design]

Apparatus 11 of the present invention to separate components of liquid samples is equipped with a generally cylindrical main body 12, holding part 13 that fits into main body 12, and separating part 14 that is held by both main body 12 and holding part 13. In main body 12, penetrating hole 16 is formed along the central axis and fitting part 18 that matches holding part 13 is created at the top. Separating part 14 is composed of an elastic and fluid-permeable material; or it may be composed of a material that swells by absorbing fluid; or it may form a hollow space that connects with penetrating hole 16, which may be filled with a serum separating agent.

[Effects]

The apparatus can separate each component of the fluid completely, without the risk of mixing the components of the upper portion with those at the lower portion. Furthermore even when the inner diameter changes within a single tube, each component can be completely separated.



[Claim]

[Item 1]

An apparatus to separate components of a fluid sample that s equipped with a generally cylindrical main body, a holding art that is fitted into the said main body, and a separating art that is held by the main body and the holding part. In the forementioned main body, a penetrating hole is created along the entral axis and a fitting part that matches the aforementioned tting part is formed at the upper section. The aforementioned eparating part is composed of an elastic and fluid-permeable aterial.

[Item 2]

An apparatus to separate components of a fluid sample that s equipped with a generally cylindrical main body, a holding art that is fitted into the said main body, and a separating art that is held by the main body and the holding part. In the forementioned main body, a penetrating hole is created along the entral axis and a fitting part that matches the aforementioned itting part is formed at the upper section. The aforementioned eparating part is composed of a material that swells by osorbing a fluid.

[Item 3]

The apparatus to separate components of a fluid sample that s defined by Item 1 or 2 wherein a hollow space that connects ith the aforementioned penetrating hole is formed in the eparating part and is filled with a serum separating agent.

[Detailed Description of the Invention]

[0001]

[Areas of Industrial Application]

The present invention concerns an apparatus that separates into individual components a fluid sample that is composed of multiple components with varied specific gravities that are not soluble in each other. Specifically, it concerns an apparatus to separate each component through a centrifugation process, in which a liquid sample is placed in a tube and is separated into various components by a centrifugal force. Furthermore the present invention concerns an apparatus to separate a fluid sample into various components even when the inner diameter of a tube changes (e.g., when the tube is tapered) or a group of tubes with various inner diameters is used. In addition, this invention concerns an apparatus to separate fluid samples into their components, using a separating part and enable complete airtightness (complete separation of components with large specific gravities from those with small specific gravities).

[0002]

[Conventional Technology]

Conventional blood tests have been conducted mainly by using serum (or plasma) that has been separated from whole-blood. Therefore as a preliminary step, it has been necessary to separate the blood sample that was collected in blood-collecting tubes (such as "spitz") into serum and plasma (hereafter called serum) and clots and blood cells. As a common practice, a whole blood sample that has been collected is placed in a blood-collecting tube such as a "spitz" and is subjected to centrifugation to isolate the serum. This centrifugal process, however, leaves the separated serum and clots in a very unstable condition. The slightest impact causes the blood cells in the clots that have precipitated to be mixed with the serum and a very careful operation is required in handling the blood samples after separation.

[0003]

Various attempts have been made to improve on this unstable state of a blood sample following separation and facilitate the test procedures. For example, there is a method which uses a thixotropic serum separating agent having a specific gravity that is between those of the serum and clots. The agent is composed mainly of a low molecular weight synthetic resin (such as silicone oil) that is characterized by a certain specific gravity and a thixotropic characteristic. During the centrifugal process, the agent is fluidized, forming a solid separating wall over the clots.

[0004]

This serum separating agent, however, is associated with the following shortcomings:

(1) If the physical properties of the aforementioned clots are not normal, a strong separating wall cannot be formed. For example, if the clots are soft and associated with a low specific gravity (as in a dialysis patient), it may not be possible to separate the serum and clots completely.

(2) Serum separating agents are hydrophobic, dissolve in water with difficulty but readily in oil-soluble drugs. Therefore in determining the drug concentration in the blood, the drug in question may be dissolved in the serum separating agent, making it impossible to obtain an accurate analytical result.

(3) A serum separating agent activates blood coagulation factors; therefore it cannot be used in tests for the analysis of these factors.

(4) The properties of blood vary among individuals. The generation of fibrin, in particular, interferes with the analysis of serum following centrifugation. Therefore it is necessary to capture the fibrin that has been generated; but the aforementioned serum separating agent is incapable of capturing fibrin. The blood from dialysis patients is particularly likely to generate fibrin but serum separating agents are unable to prevent fibrin generation.

[0005]

To eliminate these shortcomings of a serum separating agent, a serum filtering piston such as the one shown in Figure 12 has been suggested (refer to Patent Publication 51-105890). This serum filtering piston 1 is composed of discoid filter 2 having a diameter that is slightly larger than the inner diameter of the blood-collecting tube and cylindrical weight 3 that is installed at the center of the said filter 2 and has a diameter that is smaller than that of filter 2. As shown in Figure 13, blood 5 is collected in blood-collecting tube 4 and serum filtering piston 1 is inserted into blood-collecting tube 4. Through centrifugation, blood filtering piston 1 moves between serum 6 and clots 7 as shown in Figure 14. As filter 2 adheres to inner wall 4a of blood-collecting tube 4, serum 6 and clots 7 are completely separated. The serum is then removed by decantation.

[0006]

[Problems to Be Solved by the Present Invention]

However the aforementioned serum filtering piston 1 is equipped with filter 2, which is pinned by weight 3, there is a risk of filter 2 being separated. Furthermore piston 1 pulls filter 2 down. Filter 2 must be equipped with a certain strength; it slides downward along inner wall 4a of blood-collecting tube 4 while being curved. Through this motion, the filter rubs against clots that are attached to inner wall 4a, destroying blood cells and producing erroneous test results [such as in the analysis of the blood LDH (lactose dehydrogenase) level]. Furthermore, filter 2 tends to oscillate. It is, therefore, difficult to maintain filter 2 in a horizontal position and in good balance, thus causing the clots to adhere to filter 2; or the blood cells of clots 7 to move through the space between inner wall 4a of blood-collecting tube 4 and filter 2 and get mixed with serum 6 during serum collection following centrifugation.

[0007]

In another attempt to improve the shortcomings of earlier products, an elastic rubber plate is used instead of serum

filtering piston 1. However, a rubber plate resists sliding and does not move smoothly along the inner wall of the blood-collecting tube. When there is a change in the inner diameter of the tube (as in a plastic tube with an inner diameter that tapers toward the bottom), the sliding motion becomes very difficult, presenting a problem in complete separation of serum and clots.

[0008]

The present invention has been developed in response to these problems. Its purpose is to offer an apparatus that separates fluid samples that contain components with various specific gravities that are not soluble in each other. In particular, it purports to offer an apparatus to separate components of liquid samples that can separate serum and clots completely in a separation operation of blood samples.

[0009]

[Method to Solve the Problems]

To solve the aforementioned problems, the present invention adopts the following apparatus to separate components of fluid samples: The apparatus to separate the components of liquid samples defined by Item 1 of the Claim is equipped with a generally cylindrical main body, a holding part that fits with the said main body, and a separating part that is held by the main body and the holding part. In the aforementioned main body, a penetrating hole is formed along the central axis and a fitting part that matches the aforementioned holding part is created at the upper section. The aforementioned separating part is composed of an elastic and fluid-permeating material.

[0010]

The apparatus to separate fluid samples that is defined by Item 2 of the Claim is equipped with a generally cylindrical main body, a holding part that is fitted with the said main body, and a separating part that is held by the main body and the holding part. In the said main body, a penetrating hole is created along the central axis and a fitting part that matches the aforementioned holding part is formed at the upper section. The

aforementioned separating part is composed of a material that swells by absorbing a fluid.

[0011]

The apparatus to separate components of fluid samples defined by Item 3 of the Claim is one defined by Item 1 or 2; but the aforementioned separating part has a hollow section that connects with the aforementioned penetrating hole and is filled with a serum separating agent.

[0012]

[Actions]

In the apparatus to separate components of a fluid sample defined by Item 1 of the Claim, the separating part that is composed of an elastic and fluid-permeable material is held by the main body and the holding part. The fluid sample that has been collected is placed in a tube, into which the apparatus is inserted. The preparation is then subjected to centrifugation. While permitting the separated fluid components to pass through its penetrating hole and maintaining the separating apparatus in a well-balanced horizontal position, the said apparatus moves to the boundary between the separated components and holds down the lower components. Because the separating part adheres closely to the inner wall of the tube due to elasticity of the said part, the apparatus is immobilized at the desired position, thus preventing the components in the lower section from moving toward the upper components. In this manner, each component is completely separated with no risk that the components in the lower section will mix with those in the upper section. Even when the inner diameter of the tube varies, each component is completely separated.

[0013]

When this apparatus is used to separate blood components, the blood that has been collected is placed in a blood-collecting tube and left standing for blood clots to form. The apparatus is then inserted into the blood-collecting tube, which is subjected to centrifugation. While permitting the serum to pass through the

penetrating hole and maintaining the separating part in a well-balanced horizontal position, the apparatus moves to the boundary of the serum and clots and holds down the clots. Because the separating part adheres closely to the inner wall of the blood-collecting tube due to elasticity of the said part, the apparatus is retained at the desired position, preventing the clots from shifting into the serum layer. Thus the apparatus is capable of complete separation of serum and clots without the risk that the blood cells from the clots will migrate into the serum. The separating part does not slide against the inner wall of the tube while curving; instead it comes into contact gently with the inner wall due to the repulsion force that is generated following contraction in the radial direction. In this manner, no excessive compression force is applied against the wall to destroy the blood cells. Even when the inner diameter of the blood-collecting tube varies, it is possible to separate serum and clots completely.

[0014]

In the apparatus to separate components of fluid samples that is defined by Item 2 of the Claim, the separating apparatus, which is composed of a material that swells by absorbing a fluid, is held by the main body and the holding part. A fluid sample that has been collected is placed in a tube; the apparatus is inserted into this tube; and the tube is subjected to centrifugation. While allowing the separated fluid components to pass through the penetrating hole and maintaining the separating part in a well-balanced horizontal position, the apparatus moves into the boundary between the components that have been separated, while holding down the lower components. Because the separating part swells by absorbing the fluid and adheres closely to the inner wall of the tube, the apparatus is fixed at the desired position, preventing the lower components from moving into the upper components. Thus the apparatus separates each component completely and there is no risk of the lower components getting mixed with the upper components. Furthermore, each

component can be completely separated even when the inner diameter of the tube varies.

[0015]

When this apparatus is used as an instrument to separate blood components especially, the separating part that is retained by the main body and the holding part swells by absorbing the serum. Specifically, the blood that has been collected is placed in a blood-collecting tube and left standing so clots will form. The apparatus is placed in this tube, which is then subjected to centrifugation. While permitting the serum to infiltrate through the penetrating hole and maintaining the separating part in a horizontal and well-balanced position, the apparatus moves to the border between the serum and clots and holds the clots down. Because the separating part has swollen by absorbing the serum and adheres closely to the inner wall of the blood-collecting tube, the apparatus is immobilized at a predetermined position, preventing the clots from moving to the serum layer and eliminating any risk that the blood cells from the clots will become mixed with the serum. Furthermore, even if the inner diameter of the blood-collecting tube varies, the serum and clots can be completely separated.

[0016]

In the apparatus to separate components of liquid samples defined by Item 3 of the Claim, the aforementioned hollow section is filled with a serum separating agent. Thus even after centrifugation, the separating part adheres closely to the inner wall of the blood-collecting tube and the serum separating agent permeates and fills the space between the apparatus and the blood-collecting tube. Thus the apparatus completely separates the serum and clots without the risk that blood cells from the clots will mix with the serum. Because the aforementioned hollow section is filled with the serum separating agent, the area where the said agent comes into contact with the serum is extremely limited, reducing the possibility that the agent will cause the serum to deteriorate. Thus even when the blood content of an oil-

soluble drug is to be determined, the possibility of the drug being dissolved in the serum separating agent is eliminated and an accurate analytical result can be produced.

[0017]

[Examples]

Examples of the apparatus to separate components of fluid samples of the present invention are introduced in the following paragraphs.

(Example 1)

Figure 1 shows a longitudinal section of blood separating apparatus 11 (an apparatus to separate components of liquid samples) and Figure 2, an oblique view of blood separating apparatus 11 that has been disassembled. This blood separating apparatus 11 is composed of main body 12, holding part 13, and separating part 14. Main body 12 is generally discoid, wherein penetrating hole 16 having a round cross section is formed, extending from conical and curved lower surface 15 and running along the central axis of main body 12 and fitting hole 18, having a round cross section, is created extending from flat surface 17 and running along the central axis of main body 12. On the aforementioned upper surface 17, notches 19, 19, ... which become gradually deeper from the edge to the center, are formed at 4 positions, symmetrically located around the central axis. On the inner periphery of fitting hole 18, grooves 20, 20, ... are formed, extending downward from notches 19, 19, ...

[0018]

Holding part 13 is composed of cylindrical fitting projection 21, which matches the aforementioned fitting hole 18, and generally discoid holding part 22, which is formed coaxially at one end of the said fitting projection 21. It is desirable that holding part 22 tilt to form a concave surface when solid parts (e.g., blood cells) that have precipitated slip off the surface. Separating part 14 is discoid and has a diameter that is larger than that of the aforementioned main body 12. At its center, hole 23, through which the aforementioned fitting

rojection 21 is inserted, is formed.

[0019]

The aforementioned main body 12 and holding part 13 may be omposed of identical or different materials if their mean pecific gravity is intermediate between those of the serum and lood clots. Specifically, optimum materials are represented by ynthetic resins (such as polystyrene, polyethylene, olypropylene, and ABS resin) that have specific gravities anging from 1.04 to 1.08 g/cm^3 (or more preferably from 1.05 to .07 g/cm^3) or these synthetic resin materials to which inorganic aterials such as barium sulfate are added to adjust their pecific gravities. It is required that the outer diameters of he aforementioned main body 12 and holding part 13 be slightly maller than the diameter of the opening of the blood-collecting ube and the inner diameter of its bottom section so that the pparatus may move freely to the bottom of the tube.

[0020]

Separating part 14 is made of a material that permits fluid ermeation and readily stretches and contracts so that it allows he serum to pass under a centrifugal force ranging from 300 to ,500 G but prevents blood cells from passing under normal ravity. Optimum examples include expandable foamy synthetic esins with continuous pores (such as urethane and polyethylene). ibrous materials such as glass fibers, cellulose fibers, and onwoven textiles may also be used. It is desirable that these aterials for separating part 14 have a pore diameter ranging rom 50 to 500 μm and a pore percentage over 80%.

[0021]

Separating part 14 may be lightly coated with a material such as liquid silicone resin) that does not react with blood so hat the said separating part 14 may move smoothly without damaging the blood. For example, foamy urethane resin with a density of 0.074 g/cm^3 and pore percentage of 94% that has been mmersed in silicone oil (350 cs) to reduce the pore percentage o 78.7% is desirable because the elasticity of the part is well-

retained and the silicone oil is not likely to be released.

[0022]

Separating part 14 should be large enough to cover the cross section of the blood-collecting tube completely; and its outer diameter at expansion should be equal to or slightly larger than the inner diameter of the tube. The thickness of the part is not specified; but in actual practice the optimum thickness ranges from 0.5 to 3 mm so that the serum recovery rate will not be reduced when an expanded form is immersed in blood.

[0023]

By attaching separating part 14 having the above-described characteristics to main body 12 with the aid of holding part 13, the serum and clots are completely separated, while preventing sliding motion of separating part 14 due to its curvature and averting the destruction of blood cells.

[0024]

Examples to delineate the effects of blood separating apparatus 11 are described below with the aid of Figures 1 through 6. First, blood separating apparatus 11 (shown in Figures 1 and 2) was produced. In this example, the dimensions of main body 12 were: outer diameter 12, 12.8 mm; height of the outer periphery, 9.5 mm; inner diameter of penetrating hole 16, 2 mm; inner diameter of fitting hole 18, 5 mm; depth, 5 mm; width of groove 20, 1.5 mm; and depth, 1 mm. The dimensions of holding part 13 were: outer diameter of fitting projection 21, 5 mm; maximum height, 3.5 mm; outer diameter of holding section 22, 12.8 mm; and height, 5.0 mm.

[0025]

For the aforementioned main body 12 and holding part 13, ABS resin (Estylene ABS 320, manufactured by Shinnichitetsu Kagaku, Ltd.) with a specific gravity of 1.05 was subjected to injection molding to the above-specified dimensions. The actual specific gravity after assembling these parts was 1.048. For separating part 14, expanded polyurethane (Inoac Mold Filter-MF-80, manufactured by Inoac Corporation) having an actual density of

0.074 g/cm^3 and pores count of 3/mm^2 was formed into a sheet measuring 2 mm in thickness, from which disks measuring 13.5 mm in outer diameter and 5 mm in central pore diameter were punched out. For a blood-collecting tube, a commercially produced glass tube with effective capacity of 10 ml, opening diameter of 13.2 mm; inner diameter of 13.5 mm, and length of 100 mm was used.

[0026]

First, approximately 7 ml of blood 32 that had been collected was placed in blood-collecting tube 31 (Figure 3), which was left standing at ambient (26°C) for 3 hours for coagulation of blood 32 (Figure 4). Next, blood separating apparatus 11 was inserted into this blood collecting-tube 31, which was then subjected to centrifugation at 1,000 G for 5 minutes. After centrifugation, blood separating apparatus 11 was immobilized over clots 33, while serum 34 and clots 33 were completely separated (Figure 5). Furthermore serum 34 was free of clots 33 and there was no sign of hemolysis of blood cells. Next, blood-collecting tube 31 was tilted to transfer only serum 34 to another smaller glass tube. This transfer operation was conducted slowly over a period of 15 seconds for almost complete recovery of serum 34. During this operation, clots 33 did not move at all nor did any blood cells that failed to coagulate pass separating part 14 to move to the side of serum 34.

[0027]

Blood separating apparatus 41, which was composed of main body 12 and holding part 13 but without separating part 14 was prepared and subjected to the test described above under identical conditions. Following centrifugation, the blood separating apparatus was situated on clots 33 at the boundary of serum 34 and clots 33 as shown in Figure 6; but clots 33 still had a tapered top end as before centrifugation and some of serum 42 was present in clots 33. Next, this blood-collecting tube 31 was tilted to transfer only serum 34 to another small glass tube. Within one or two seconds, uncoagulated blood cells moved to the side of serum 34. It was extremely difficult to collect serum 34

ıly.

[0028]

As explained above, blood separating apparatus 11 of the irst example is equipped with generally cylindrical main body 2, holding part 13 that fits with main body 12, and separating art 14 that is held by main body 12 and holding part 13. In main ody 12, penetrating hole 18 is formed along the central axis and itting hole 19, which matches with fitting projection 21 of the foremention holding part 13, is created on upper surface 15. ıe aforementioned separating part 14 is composed of an elastic ıd fluid-permeable material and is capable of completely eparating serum 34 and clots 33, thus improving the yield of erum 34 and eliminating the risk of blood cells from clots 33 ixing in serum 34. In addition, serum and clots can be ompletely separated even when the inner diameter of blood- ollecting tube 31 varies. Main body 12, holding part 13, and eparating part 14 are composed of a macromolecular material that s inactive against blood; and even after extended storage, no nteractions between the serum components and these parts take lace (e.g., adsorption or leaching), enabling highly accurate nalysis.

[0029]

(Example 2)

Figure 7 shows a longitudinal section of blood separating pparatus 51 of the second example. In this blood separating pparatus 51, main body 12, holding part 13, and separating part 4 were slightly altered from those of the aforementioned blood eparating apparatus 11. This blood separating apparatus has a enerally cylindrical main body 52, also generally cylindrical olding part 53, and discoid separating part 54. In main body 52, enetrating hole 56, having a round cross section, is formed, xtending from conical and curved lower surface 55 and running long the central axis of main body 52; on flat upper surface 57, itting holes 58 and 58 are formed at symmetrical positions, with he central axis of main body 52 at their center.

[0030]

In holding part 53, penetrating hole 60, having a round cross section, is formed, extending from conically curved upper surface 59 and running along the central axis of holding part 53; on flat surface 61, cylindrical fitting projections 62 and 62, which match with fitting holes 58 and 58, are formed at positions symmetrical to the central axis of holding part 53. Separating part 54 is a disk with a diameter that is larger than that of main body 52. At positions symmetrical to the central axis of this separating part 54, holes 63 and 63, into which fitting projections 62 and 62 are inserted, are formed. This blood separating apparatus 51 is associated with the action and effects of the above-described blood separating apparatus 11.

[0031]

(Example 3)

Figure 8 shows a longitudinal section of blood separating apparatus 71 of Example 3 and Figure 9, the bottom surface of the same apparatus. In these figures, the components that are identical to those of blood separating apparatus 11 of Figure 1 are given identical codes and their explanations are omitted. This blood separating apparatus 71 is composed of main body 72, holding part 13, and separating part 14. Main body 72 is generally cylindrical, in which penetrating hole 16, having a round cross section, is formed, extending from conically curved lower surface 15 and running along the central axis of main body 72; and on lower surface 15, crisscrossing grooves 73, 73, ... are created with penetrating hole 16 at their center to permit the upward release of air and serum around this surface. On upper surface 17 and fitting hole 18, grooves 74, 74, ... are formed at 4 locations that are symmetrical to the central axis. In the aforementioned penetrating hole 16, hollow section 75 is formed to connect with the said penetrating hole 16. This hollow section is filled with a liquid sealant 76 (serum separating agent) that is inactive against blood (such as a silicone oil) with a specific gravity that has been adjusted to be intermediate

between those of serum and clots.

[0032]

When this blood separating apparatus 71 is inserted into a blood-collecting tube, which is then subjected to centrifugation, the said blood separating apparatus 71 moves to the border between the serum and clots due to the centrifugal force. The subsequent and continuous centrifugal force replaces sealant 76 with serum. Sealant 76 seeps out through groove 74 and then outside blood separating apparatus 71, filling the space between blood separating apparatus 71 and the blood-collecting tube. Thus this blood separating apparatus 71 completely separates the serum and clots, eliminating the risk of the blood cells from the clots getting mixed with the serum. When the blood content of an oil-soluble drug is to be determined, there is no likelihood of the drug dissolving in the serum separating agent and accurate data can be obtained.

[0033]

In this instance, it is possible to separate serum and clots without separating part 14. However, there may be an instance when contact between hydrophobic sealant 76 and serum may reduce the blood concentration of a fat-soluble drug that resists dissolution in water, thus hindering accurate analysis of the drug. Therefore the presence of both separating part 14 and sealant 76 enables an accurate analysis.

[0034]

This blood separating apparatus 71 is also associated with actions and effects similar to those of the above-cited blood separating apparatus 11; yet the aforementioned hollow section 75 is filled with sealant 76, thus drastically reducing the area of contact between this sealant and the serum and eliminating the possibility of degrading the serum. Therefore in determining the blood concentration of a fat-soluble drug, an accurate analysis is possible. In addition, the need to form grooves 73, 73, ... is eliminated if lower surface 15 is in a concave form with the projection turned downward.

[0035]

(Example 4)

Figure 10 shows a longitudinal section of blood separating paratus 81 of Example 4, in which separating part 14 of the ove-described blood separating apparatus 11 is replaced by elling part 82. The other key elements are completely identical those of blood separating apparatus 11. This swelling part 82 composed of an expanding rubber that gradually swells through ntact with serum. In an optimal example, 10 to 60 weight parts a water-absorbing resin, such as sodium acrylate polymer, a ponified product of vinyl acetate-acrylic acid ester copolymer, d isobutylene-maleic anhydride copolymer, is added to 100 ight parts of EVA resin containing 28% vinyl acetate. The two e mixed well and pressed into a sheet form, from which disc rms are punched out.

[0036]

The above-cited swelling part 82 is devoid of liquid-rmeability and pliability that is associated with expanded ethane. Therefore if swelling part 82 is larger than the blood-llecting tube, the apparatus moves with great difficulty and it comes impossible for the serum to move during centrifugation. us it is desirable that the outer diameter of the part before elling be slightly smaller than the inner diameter of the ood-collecting tube. If the material is such that the part ells instantly when it comes into contact with the serum before ntrifugation, swelling part 82 may not move in spite of ntrifugation. Therefore it is desirable that the material be ie that gradually swells in contact with the serum to a size ceeding the inner diameter of the blood-collecting tube so that will press against the inner wall of the blood-collecting tube ter centrifugation. Normally, a blood sample is centrifuged for to 10 minutes to separate the serum and clots. It is desirable, ierefore, to use a swelling rubber that completes the expanding ocess in 5 to 15 minutes following immersion in serum.

[0037]

When this blood separating apparatus 81 is inserted into a blood-collecting tube immediately before centrifugation and then the preparation is subjected to centrifugation, the said blood separating apparatus 81 is moved to the border between the serum and clots by the centrifugal force. At this moment, the swelling rubber begins to absorbs serum and expands. The vertical direction is defined by fitting main body 12 and holding part 13 and swelling takes place in the radial direction. As shown in Figure 1, the swelling part presses against inner wall 31a of blood-collecting tube 31, forming a complete separating wall between the serum and clots. This blood separating apparatus 81 is also associated with actions and effects similar to those of the above-cited blood separating apparatus 11.

[0038]

In the above-cited examples, the separating apparatus was used to separate blood components. However, the present invention is not limited to this purpose. It may be applied to various areas such as:

(1) Extraction of solvents for substances such as heavy metals in the analyses of waste water;

(2) Isolation and purification of enzymes;

(3) Isolation, extraction, and purification of chemical components; and

(4) The aqueous biphasic partition method used in separating various cellular components, such as mitochondria and chloroplasts.

[0039]

[Effects of the Present Invention]

As described above, the separator of the components of fluid samples defined by Item 1 of the Claim is equipped with a generally cylindrical main body, a holding part that fits with the said main body, and a separating part that is held by the main body and holding part. In the aforementioned main body, a penetrating hole is formed along the central axis and a fitting

part that fits with the aforementioned holding part is created at the upper section. The aforementioned separating part is made of an elastic and liquid-permeable material and is capable of completely separating the components of the fluid, thus eliminating the possibility that the components of the upper section will mix with those of the lower section. In addition, complete separation of components is possible even when the inner diameter of the tube changes.

[0040]

When this apparatus is applied to separate blood components, in particular, the serum and clots are completely separated, thus improving the rate of serum recovery and eliminating the risk that the blood cells from clots will mix with the serum. Furthermore the serum and clots are completely separated even when the inner diameter varies.

[0041]

The apparatus to separate components of fluid samples defined by Item 2 of the Claim is equipped with a generally cylindrical main body, a holding part that fits with the said main body, and a separating part that is held by the main body and the holding part. In the aforementioned main body, a penetrating hole is formed along the central axis and a fitting part that fits with the aforementioned holding part is created at the upper section. The aforementioned separating part is composed of a material that swells by absorbing a fluid: it is capable of complete separation of the components of the fluid without the risk that the components of the lower section will mix with those of the upper section. In addition, each component is completely separated even when the inner diameter varies.

[0042]

When this separating apparatus is applied to separate blood components, it becomes possible to separate the serum and clots completely, thus improving the rate of serum recovery and eliminating the risk that the blood cells from clots will migrate into the serum. In addition, the serum and clots are completely

separated even when the inner diameter varies.

[0043]

According to the design of the apparatus for separating components of fluid samples of Item 3 of the Claim, a hollow section that connects with the aforementioned penetrating hole is formed in the apparatus and the said hollow section is filled with a serum separating agent. Thus the area of the serum separating agent in contact with the serum is drastically reduced, eliminating the risk of degrading the serum. In determining the blood concentration of a fat-soluble drug, there is no risk of the drug dissolving in the serum separating agent, enabling an accurate analysis. In addition, it is possible to separate the serum and clots completely even when the inner diameter varies.

[Brief Description of Drawings]

[Figure 1]

A longitudinal section of blood separating apparatus (an apparatus to separate components of a fluid sample) of Example 1 of the present invention.

[Figure 2]

An oblique view of the disassembled blood separating apparatus of Example 1 of the present invention.

[Figure 3]

A figure showing the process of centrifugation of blood using the blood separating apparatus of Example 1 of the present invention.

[Figure 4]

A figure showing the process of centrifugation of blood using the blood separating apparatus of Example 1 of the present invention.

[Figure 5]

A figure showing the process of centrifugation of blood using the blood separating apparatus of Example 1 of the present invention.

[Figure 6]

A figure showing the process of centrifugation of blood sing a blood separating apparatus without the separating part.

[Figure 7]

Vertical section of the blood separating apparatus of xample 2 of the present invention.

[Figure 8]

Vertical section of the blood separating apparatus of xample 3 of the present invention.

[Figure 9]

The lower surface of the blood separating apparatus of xample 3 of the present invention.

[Figure 10]

A vertical section of the blood separating apparatus of xample 4 of the present invention.

[Figure 11]

A vertical section of the blood separating apparatus of xample 4 of the present invention, showing the manner by which he swelling section expands.

[Figure 12]

An oblique view of a conventional serum-filtering piston.

[Figure 13]

A process of centrifugation of blood using a conventional erum-filtering piston.

[Figure 14]

A process of centrifugation of blood using a conventional erum-filtering piston.

[Explanation of Codes]

11. blood separating apparatus (an apparatus to separate omponents of a liquid sample)

12. main body

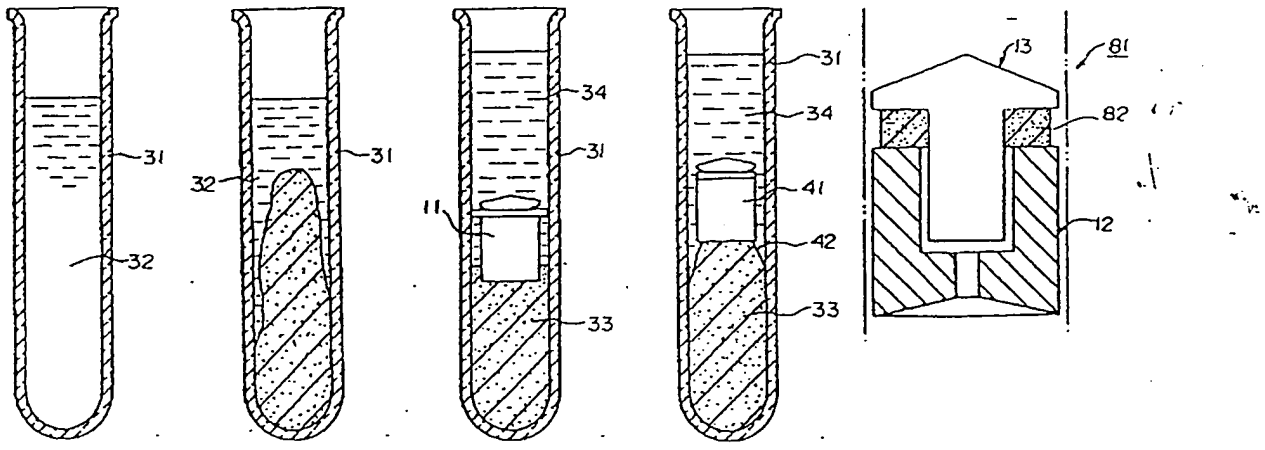
13. holding part

14. separating part

16. penetrating hole

18. fitting hole
21. fitting projection
22. holding section
31. blood-collecting tube
32. blood
33. clots
34. serum
51. blood-separating apparatus
52. main body
53. holding part
54. separating part
56. penetrating hole
58. fitting hole
60. penetrating hole
62. fitting projection
71. blood-separating apparatus
72. main body
75. hollow section
76. sealant (serum separating agent)
81. blood-separating apparatus
82. swelling part

[Fig. 3] [Fig. 4] [Fig. 5] [Fig. 6] [Fig. 10]



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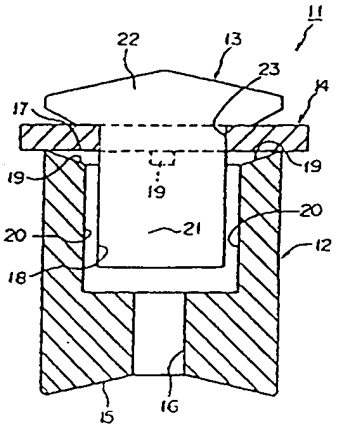

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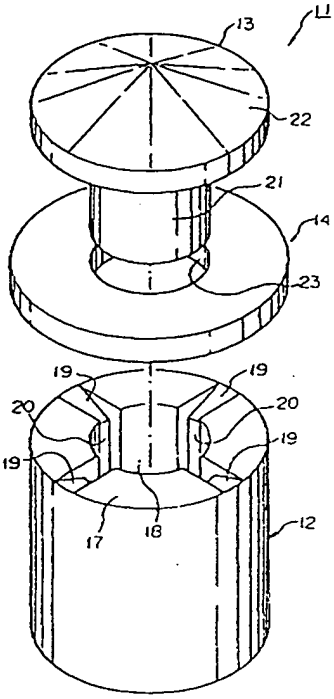

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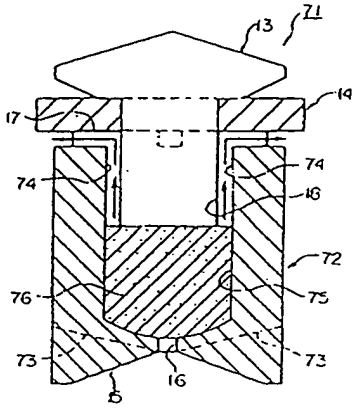

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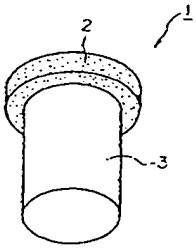

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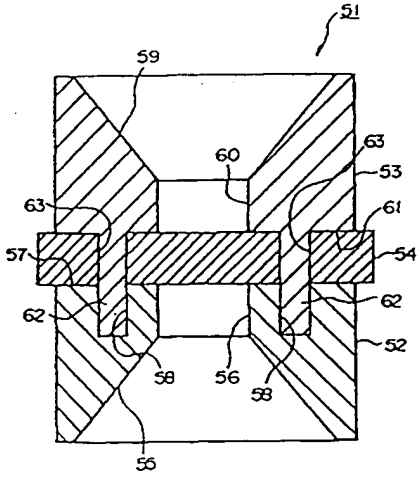

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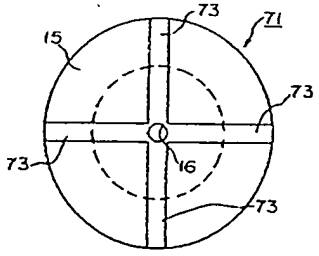
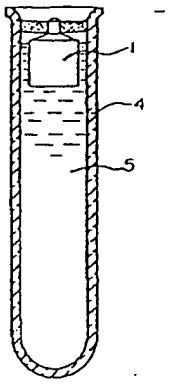
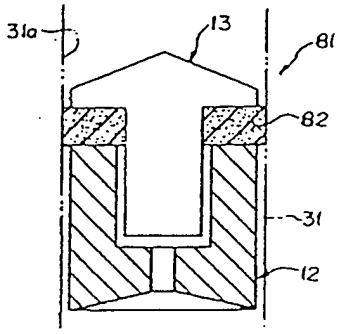


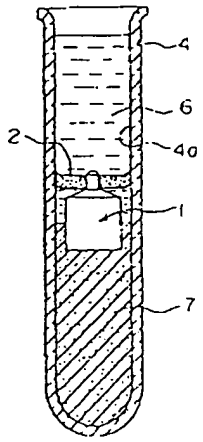
【図１３】



[Fig. 11]



[Fig. 14]



[Procedural Modification]

[Date of Submission]

August 6, 1993

[Modification 1]

[Name of Document to Be Modified]

Specification

[Item to Be Modified]

0037

[Method of Modification]

Change

[Content of Modification]

[0037]

When this blood separating apparatus 81 is inserted into a blood-collecting tube immediately before centrifugation and then the preparation is subjected to centrifugation, the said blood separating apparatus 81 is moved to the border between the serum and clots by the centrifugal force. At this moment, the swelling rubber begins to absorbs serum and expands. The vertical direction is defined fitting of main body 12 and holding part 13 and swelling takes place in the radial direction. As shown in

Figure 1, the swelling part presses against inner wall 31a of blood-collecting tube 31, forming a complete separating wall between the serum and clots. This blood separating apparatus 81 is also associated with actions and effects similar to those of the above-cited blood separating apparatus 11. For swelling part 82, any material that swells gradually by coming into contact with serum may be used. In addition to the aforementioned swelling rubber, materials such as a cellulose sponge can produce the same effects and actions. This cellulose sponge is an expanded body having cellulose as its main component. In a dry state, it contracts; but when in contact with a fluid such as serum, it swells by absorbing the said fluid. For an optimum example, cellulose that is obtained from wood is combined with a small amount of a reinforcing material; the preparation is molded, heated, coagulated, compressed to form a sheet, and cut into a discoid form. The cellulose sponge swells instantly when it comes into contact with an aqueous solution; and when it is used in the separation of serum, there is a possibility that the blood separating apparatus will not reach the border between the serum and clots during the centrifugal process. For this reason, it is desirable that the cellulose sponge be pretreated for a delayed foaming effect. For the delayed foaming process, a dry cellulose sponge may be immersed in a resin that does not affect the analytical result—e.g., hydrophobic resins (such as liquid silicone oil and polybutene) and hydrophilic resins [such as polyethylene glycol (PEG) and polyvinyl alcohol (PVA)]. In another method, the surface of the cellulose sponge is lightly coated with a hydrophilic polymer film. By subjecting it to these processes, the cellulose sponge can swell after any desired time lapse following immersion in the serum. For example, a cellulose sponge that has been subjected to the delayed foaming process by impregnating it with an equal weight of polybutene having a mean molecular weight of 2,400 and viscosity of 4,600 CST (centistokes) at 98.9°C is immersed in serum and allowed to undergo a gradual swelling process over 4 minutes. Another

advantage of impregnating the cellulose sponge with a liquid resin is to prevent blood cells from migrating from the clot layer to the serum layer.